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Will neuroscience account for the psychotherapeutic outcome in schizophrenia?

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Summary

Neuroscientific research explaining the effectiveness of psychotherapy went in three directions. The first, basing on a theory of explicit (declarative, conscious) and implicit (procedural, subconscious) memory aims at reinterpretation of the mechanisms of psychotherapy. This method is useful in analysing effects of cognitive psychotherapy but also psychoanalytically oriented psychotherapy which is based on interpretations and insight.

The second current in such research is connected with the possibility of neuroimaging, which allows to evaluate changes occurring in the course of therapy. This method enables to show biological mechanisms of therapeutic alliance or reduction of basic anxiety. In the third category of studies, changes in cerebral metabolism that occur due to psychotropic medication and psychotherapy are observed with the aid of neuroimaging. Here, the findings are extremely interesting, for instance, in treatment of depression psychotherapy brings about more specific changes than anti-depression drugs. Most of the investigation is focused on the effects of psychotherapy for patients suffering from depression and obsessive-compulsive disorder because of high homogeneity of these disorders. Schizophrenia-related disorders are less homogeneous, and owing to that drafting a research plan is a much more complicated task. So the path towards neuroscience, which may account for the effects of psychotherapy, is still unexplored.

schizophrenia / neuroscience / psychotherapy

INTRODUCTION

Since the early twentieth century, no agreement has been reached among psychiatrists nor conclusive scientific evidence has been found to corroborate Kraepelin's hypothesis concerning the nosological homogeneity of disorders that, following Bleuler, are termed as "schizophrenia". Within the period of almost one hundred years after Bleuler's publication, a number of new approaches and concepts have emerged so as to elucidate the nature of the disorder; nowadays, under the influence of American psychiatry, the majority of psychiatrists use the term introduced by Bleuler to refer to the disorder as viewed by Kraepelin, who called it *dementia praecox*.

Despite the discord as to the boundaries, nature, and symptoms adopted as diagnostic criteria, some compromise, however, has been attained. It pertains to the complex pathogenesis of the disorder. In the 1960's it was assumed that the disorder is due both to biological and psychosocial factors, the former being responsible for the individual proneness to develop the disorder, the latter – for the onset. In discussions of the origins and dynamics of schizophrenia-like disorders, the vulnerability-stress hypothesis was applied in order to formulate, among others, the theoretical basis of the concept of integrated treatment or, as Alanen terms it [1],

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needs-adapted treatment. Its multiple variants embrace pharmacotherapy, psychotherapy, family therapy, a system of community and social services.

As compared to other elements of integrated treatment, pharmacotherapy is based on well-researched effects of chemical substances and theoretical models of the pathogenesis of the disorder. The latter include the hypothesis concerning the role of neurotransmitters in schizophrenia and the explanation of the effects of medication obtained through modulation of neurotransmission. These theories can be operationalised and verified via experiments, e.g. checking animal models of the disorder. They also provide a starting point for the synthesis of new medicines. Theoretical foundations of the remaining elements of integrated treatment are a slightly different case. Psychological and sociological concepts of the origins of schizophrenic disorders, including the 1970's anti-psychiatric negation of their occurrence, attractive as they may seem, did not comply with academic discipline, which is imperative in contemporary medicine. The persuasiveness of scientific arguments and unquestionable efficiency of anti-psychotic medication in alleviating the symptoms of schizophrenic disorders made it easier to forget that the neurotransmission theory required a limited, narrow field of observation: selected chemical substances. Indeed, this model of schizophrenia which is based on neurotransmission theory brings schizophrenia down to a metabolic disease of the brain.

According to many schizophrenia researchers, this is an excessive reduction as it excludes the explanation of cerebral functioning in illness and good health. Alanen, quoting Fleck, was unwilling to perceive human functioning as a laboratory flask [1]. The introduction of the idea of needs-adapted treatment of schizophrenia summed up his long-standing clinical psychiatric practice and research as well as knowledge of recently implemented organisational changes in the treatment of people with schizophrenia-related diseases. The mentioned changes were aimed at the application of a wide spectrum of therapeutic methods: from psychoanalytically-oriented psychotherapy to systemic family therapy and community support, with pharmacotherapy still present. Since long, a comprehensive, integrated, holistic therapeutic approach seemed to be the only sensible solution in the treatment of patients with schizophrenia-like disorders. Also Kępiński [2, 3] gave similar treatment guidelines, based on the presupposition that it is possible to account for human functioning, both in illness and good health, within the framework of interpersonal relations and functional cerebral structures. In the 1960's Kępiński attempted to create a biological model of mental functions, which he called a model of information metabolism.

Alanen, Kępiński and Fleck could not consider the neurotransmission model as adequate because their psychiatric thinking had solid humanist foundations. The developments of neuroscience, from an entirely different perspective, prove that they were right. The knowledge which has accumulated throughout the last decade makes us abandon the hope that schizophrenia-related disorders could be explained by the presence of one genetic mutation. Molecular genetics make us realize that the memory matrix included in the chemical structure of the gene allows for the construction of proteins and functional neuronal connections. But the initiation of its activity and the type of this activity both depend on the environment. Moreover, it is not solely the chemical environment, which provides the necessary substrates for the synthesis, but the entirety of environmental influences. This was confirmed by research on the impact of stress on gene expression.

Another significant contribution, which expanded our understanding of the links between cerebral functions and environmental impact, is the findings of neuroscience on the mother-child relation and the development of functional brain structures. The research is done mainly on animals, but also – whenever non-invasive methods can be applied – on humans and supplies evidence as to the effect of the mentioned relation on neuronal connections between the amygdala and pre-frontal cortex [4, 5], as well as on the neuro-hormonal efficiency in response to stress. These detailed data (which may be also deemed fragmentary) support previous research findings that pointed to the increased risk of schizophrenia among people who were deprived of parental contact in childhood. As established by Agid et al. [6], this risk grew 3.8 times higher when

somebody lost a parent before they turned 17, and 4.3 times higher when the loss was suffered before the age of 9. The importance of these scientific achievements lies in that they bridge the gap between the biological and psychological approach towards mental disorders and their treatment.

Even more interest may be attracted by the interpretation based on research findings by Kandel [7] concerning memory. The discovery that memory stimulates the expression of genes (as influenced by experience, i.e. learning) that are responsible for the synthesis of proteins which allow neurons to function won him the Nobel Prize. Kandel's reduction was to choose the simplest available animal brain to investigate learning processes, based on memory. It was the brain of a sea snail. The brain of *Aplysia*, as opposed to the brain of humans, is obviously uncomplicated. And of course nobody has studied schizophrenia in snails. Nevertheless, with the use of this model Kandel managed to prove that learning entails biological, functional and structural changes.

Empirical studies, aiming to account for the efficiency of psychotherapy from the neuroscientific perspective, are relatively well-advanced. Generally, they fall into three categories. (i) Based on the theory of explicit memory (declarative memory, consciousness) and implicit memory (procedural memory, subconsciousness) – which are concepts derived from the findings of neuroscience and used for its purposes – the mechanisms involved in psychotherapy are being revised. This method turns out to be useful in the investigation of behavioural and cognitive therapy as well as analytical therapy, relying on interpretations and working-through [8]. (ii) Another line of research resorts to functional neuroimaging and, experimentally, assesses changes in the functions of the brain that occur either in a therapeutic setting or due to psychotherapy. This allowed to shed light on biological mechanisms of interpersonal therapeutic relationship and to prove, for instance, the reduction of basic anxiety through psychotherapy. (iii) In the third category of studies, changes in cerebral metabolism are observed with the help of neuroimaging, which occur due to psychotropic medication and psychotherapy. Here, the findings are extremely interesting: for instance, in treatment of depression, psychotherapy brings about more specific changes than anti-depression drugs [9].

PSYCHOTHERAPY IN TREATMENT OF SCHIZOPHRENIA-DIAGNOSED PATIENTS

Clinical practice and results of longitudinal prospective studies on the course of schizophrenia-related disorders [1] tend to support the advantages of integrated treatment, comprising psychotherapy. This kind of treatment was used based on various theoretical premises, in a number of forms and modalities. And it seems none of modern (twentieth-century) psychotherapeutic methods has proclaimed to be inefficient.

Those psychotherapeutic techniques have been critically evaluated whose application requires that patients should be burdened with the stress involved in problem-solving, for instance when they become aware of an internal conflict and work through in psychoanalytical therapy. As the vulnerability-stress theory points to the reduced ability of coping with stress, it appears obvious that during treatment one should avoid situations that increase the risk of psychological decompensation under stress. Even in psychodynamic therapies, just a few approaches permit the aggravation of stress owed to interpretations, but on condition that a thorough preliminary examination is performed. The profundity of intra-psychological conflict, supposedly underlying schizophrenia, is – by definition – a contraindication to adopt such an approach (e.g. short-term anxiety provoking psychotherapy).

The recent years have witnessed a growing popularity of these psychotherapeutic activities that (i) favour the patients' engagement, broaden their knowledge about the illness, treatment methods and prevention of relapses, such as psychoeducation; (ii) improve the quality of life for the patients and their immediate community, such as family therapy, cognitive and behavioural therapy, and long-term group therapy with various non-specific modalities (e.g. art).

Regardless of theoretical foundations of a particular psychotherapeutic intervention, the role of non-specific psychotherapeutic

factors is emphasised: emotional support on the part on the therapist, a sense of safety in individual and group relations, a sense of meaningfulness of therapeutic activity.

This is especially conspicuous in the findings of the Kraków longitudinal study: the subjective satisfaction derived from the therapeutic relationship seems to be one of the most important predictors for the course of the illness [10]. Alanen [1] goes even further in his conclusions when searching for indications how to adapt the type of psychotherapy to the needs of the patient and to identify this one that is likely to give the patient a sense of safety and support in each individual case.

RESEARCH ON THE EFFECTS OF PSYCHOTHERAPY IN THE TREATMENT OF SCHIZOPHRENIA

It is an extremely demanding, if not impossible, task to prepare a standard assessment of the effects of psychotherapy in the treatment of schizophrenia. The findings of research programmes that evaluated the efficiency of psychodynamic psychotherapy, even preceding pharmacotherapy, were not optimistic. Our own study conducted in Kraków, which aimed at the assessment of the efficiency of group therapy in the treatment of schizophrenia-diagnose adolescents [11] (the therapy being based on the naturalistic method,) showed that in a five-year follow-up the therapeutic goal was achieved, namely an improvement was observed in the subjective need for interpersonal contact. At the same time, we did not observe any improvement in the skills required to fulfil the need. Additionally, the changes were not correlated with the further course of the disorder. Yet, the findings of this study, as well as of other, more sophisticated researched programmes concerning the efficacy of psychotherapy in schizophrenia treatment, as discussed by Alanen [1], are extremely hard to interpret, primarily because psychotherapy is one of the elements of integrated treatment. Another programme, run in Kraków [12], aimed at the assessment of the efficacy of psychotherapy in schizophrenia treatment, provided comparisons concerning a random sample of patients who underwent treatment within different treatment programmes, where the difference was the proportion of group therapy and early rehabilitation. The long-term observation led to the conclusion that psychotherapeutic components of the treatment programme have a favourable impact on the course of the illness if they take into account defined individual indications.

These findings were implemented in clinical practice: therapeutic programmes were adapted to individual needs. In particular, in long-term community programmes [13, 14], the following factors were considered: assistance in building the network of social support, working with the families, rehabilitation efforts to help find employment, support for social activities. The validity of this psychotherapeutic attitude, diversified and yet integrated, is corroborated by the beneficial outcomes, as gauged by the quality of life [15]. The findings obtained in Kraków belong to those that confirm the practicality of psychotherapy in schizophrenia treatment. Moreover, they also support the conviction about the purposefulness of adapting psychotherapeutic activities to the needs and capabilities of the person receiving treatment as well as the belief that psychotherapy should be placed within a comprehensive treatment and rehabilitation programme.

Therefore the question that ought to be posed now concerns the mechanisms that are responsible for the therapeutic effect. Depending on the basic system of theoretical assumptions for psychotherapy, we can either refer to the psychoanalytical idea of the reconstruction of the ego and strengthening its defence mechanisms, or to the neo-psychoanalytical concept of the reconstruction of the self and the ability to form a relation with the object, or – based on the assumptions of the theory of learning – seek the solution in acquisition of socially more efficient behaviours, or, lastly, find the possibilities of reducing negative emotions in the change of cognitive stereotypes.

Let us illustrate the point by checking whether and how the ways of coping with difficult situations change during therapy. The vulnerability-stress theory sees psychotherapy as a means to modify the ways of coping with stress so that they are more efficient.

This study was conducted in day hospital, where the psychotherapeutic component em-

braces everyday community meetings, everyday group psychotherapy (whose aim is communication and better insight into the illness) as well as activities that require non-verbal expression and improve social competence (e.g. movement therapy, dance, social skills training, psychodrawing and milieu therapy). At the same time, each patient remains in individual therapy, which is adapted to his/her needs and capabilities. Changes in the repertoire of defence mechanisms were assessed with the DSQ 40 [16], pre- and post-treatment assessment was conducted, and changes in psychopathology were measured with the PANSS [17]. As expected, the findings showed a statistically significant improvement in the use of mature defence mechanisms by the subjects. Besides, it was found that the lower level of negative symptoms, according to PANSS, and better use of mature defence mechanisms at the beginning of treatment were predictors of more favourable outcomes. On the other hand, no correlation was observed between the improved use of defence mechanisms and the attenuation of symptoms.

This study has left the authors in a state of confusion about the findings, which is often the case in research on treatment outcomes. Better predisposed people have more gains and better outcomes. But still the question is why ...

There is a possibility that the answer may lie in the role of non-specific features of psychotherapy, and in particular those circumstances that allow the patient to find a sense of safety and support in the therapeutic relationship.

Neuroscience and imaging technology, investigating the functions of the brain, give us hope that answers will be found to several vital questions. As caused by interpersonal psychotherapy, in depressive patients normalisation changes were observed in the metabolism of the pre-frontal cortex, caudate nucleus and thalamus (decrease), and temporal lobe (increase) [18]. In patients with the obsessive-compulsive syndrome, lower metabolic activity was observed in the right caudate nucleus following behavioural therapy [19]. It can be cautiously inferred, on the basis of these findings, that psychotherapy impacts the activity of functional cerebral structures that regulate emotions, mainly anxiety. So perhaps it is possible to prepare a standard assessment for the changes in the distribution and dynamics of brain activity in schizophrenia-diagnosed patients during and after psychotherapy. It seems, anyhow, understandable, that hitherto research focused on the effects of psychotherapy for patients suffering from depression and obsessive-compulsive disorder: schizophrenia-related disorders are less homogeneous, and owing to that drafting a research plan is a much more complicated task. And the path towards neuroscience, which may account for the effects of psychotherapy, is hardly visible yet.

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